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EXAMINER

JIANG, DONG

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1646

DATE MAILED: 08/20/2003

10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/075,846

Applicant(s)

FEDER ET AL.

Examiner

Dong Jiang

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 June 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 20-40 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 20-40 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED OFFICE ACTION

Applicant's preliminary amendment in paper No. 9, filed on 11 June 2003 is acknowledged and entered. Following the amendment, all of the original claims 1-19 are canceled, and the new claims 20-40 are added.

Currently, claims 20-40 are pending and under consideration.

Applicants submission of IDS references listed on PTO-1449, paper No. 5, is acknowledged. It is noted that the relevance of references AS and AT on page 1, and AA and AB on page 2 cannot be assessed as the references are amino acid or nucleotide sequences, and no indication of relevance or alignment to the disclosed sequences has been provided.

Objections and Rejections under 35 U.S.C. §101 and §112:

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 20-40 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a credible, substantial, specific, or well-established utility.

Claims 20-40 are directed to an isolated nucleic acid having SEQ ID NO:3, or encoding a human polypeptide of SEQ ID NO:4, a vector and a host cell thereof, and a method of recombinant expression of such. Said polypeptide is a putative glycine receptor $\alpha 4$ subunit splice variant (HGRA4sv) as it shares sequence homology with other known glycine receptor α subunits (page 38, the last paragraph), and it is designated HGRA4sv.

The specification discloses two nucleic acids, SEQ ID NO:1 and 3, which encode a putative glycine receptor $\alpha 4$ subunit (HGRA4) having SEQ ID NO:2, and a splice variant thereof (HGRA4sv) having SEQ ID NO:4. The nucleic acid sequences were identified using known ion channel sequences to search the human genomic sequence database (Example 1, page 221).

Based on the sequence similarity to known glycine receptor alpha subunits, the functional property of known glycine receptors, and the expression pattern of HGRA4sv, the specification

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asserts that HGRA4 and/or agonists or antagonists thereof would be useful for treating, detecting, and/or ameliorating disorders or diseases of the nervous system; may also play a role in modulating longitudinal muscle/myenteric plexus contraction, and various gastrointestinal disorders (page 43, the second paragraph), and in modulating inhibitory neurotransmission (page 43, the third paragraph); useful in diagnosing, treating, prognosing, and/or preventing cardiovascular diseases (page 44, the third paragraph), and other diseases and disorders such as those listed on pages 44-47.

The asserted utilities are not considered to be substantial because the specification fails to disclose any particular function, or biological significance *directly* associated with the instant HGRA4, nor any particular gene mutation, or any disease or condition associated with the HGRA4. Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a known protein. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39, see entire article, especially Box 2) states that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Doerks et al. (1998, Trends in Genetics 14:248-250) states that overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologues must have different molecular and cellular functions. In the case of the transforming growth factor (TGF) family, Vukicevic et al. (1996, PNAS USA 93:9021-9026) disclose that OP-1, a member of the TGF- family of proteins, has the ability to induce metanephrogenesis, whereas closely related TGF- family members BMP-2 and TGF- 1 had no effect on metanephrogenesis under identical conditions (p. 9023, paragraph bridging columns 1-2). Furthermore, IL-18 receptor (IL-18R) was thought to be another IL-1 receptor (IL-1R) base on the sequence homology, and therefore, designated IL-1 receptor-related protein (IL-1Rrp) when it was first discovered, and its ligand was unknown (Parnet et al., J. Biol. Chem., 1996, 271(8): 3967-70). IL-1Rrp is now known as IL-18R, has distinct ligand, and possesses distinct function

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from IL-1R even though it is a member of IL-1R family. In the instant case, applicants indicate that HGRA4 is structurally related to glycine receptor alpha subunits, which are known to form functional glycine receptor with other glycine receptor alpha subunits. However, an established utility for other glycine receptor alpha subunits cannot be automatically applied to HGRA4 without functional analysis. Even the instant specification indicates that the *exact* biological function should be tested, as stated on page 47, lines 10-13, that it is believed the encoded polypeptide *may* share at least some biological activities with glycine receptor alpha subunits, and a number of methods of determining the *exact* biological function are known in the art or described elsewhere herein. While it is likely that the HGRA4 is a glycine receptor alpha subunit, that by itself does not suggest any substantial utility for the reasons above.

Each of the disclosed utilities requires additional knowledge about the claimed nucleic acid and the protein encoded thereby before the nucleic acid or protein can be used for a specific purpose, such as those set forth in the specification. The disclosed uses in diagnosis and treatment are not substantial, in the absence of knowledge of any disease or condition associated with inappropriate HGRA4 activity or levels, which could be so treated. Therefore, there is no immediately evident patentable use for the HGRA4. Upon further research, a specific and substantial utility might be found for the claimed isolated nucleic acid or protein. This further characterization, however, is part of the act of invention, and until it has been undertaken, the claimed invention is incomplete.

The instant situation is analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an

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invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . . [i]t is not a reward for the search, but compensation for its successful conclusion.

The instant claims are drawn to a nucleic acid encoding a HGRA4sv polypeptide. There is no evidence of record or any line of reasoning that would support a conclusion that said HGRA4sv wsd, as of the filing date, useful for treatment of any disorders as stated at pages 44-47 of the specification. Until some actual functional property or specific relationship between gene mutations of HGRA4sv and diseases or conditions can be established, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility and the claimed invention is incomplete as of the filing date.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-40 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial or credible utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

In addition, even if there were utility and enablement of the nucleic acid of SEQ ID NO:3, or the polypeptide encoded thereby (SEQ ID NO:4), enablement would not be commensurate in scope with the claims, which encompass nucleic acid encoding a polypeptide 97% to SEQ ID NO:3 or the sequences encoding SEQ ID NO:4 (claim 37, for example), or fragments of the nucleic acid sequences encoding fragments of SEQ ID NO:4 (claim 20, part (e), and claims 28 and 29, for example), and antisense polynucleotide (claim 20, part (f)).

The specification discloses two nucleic acid molecules, SEQ ID NO:1 and 3, encoding amino acid sequences with particularity, HGRA4 of SEQ ID NO:2, and HGRA4sv of SEQ ID

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NO:4. No other HGRA4 variants or fragments meeting the limitations of these claims were ever identified or particularly described. The specification does not teach how to use nucleic acid variants or fragments. Since no specific biological function of HGRA4sv is disclosed in the specification, and since one skilled in the art could not determine with a reasonable expectation of success, and without undue experimentation what a specific biological function of HGRA4sv would be, the skilled artisan would not be able to make the % variants, fragments or antisense, and test them for a biological activity, or loss thereof (by antisense, for example). Furthermore, the specification provides no guidance as to how the skilled artisan could use an inactive HGRA4sv variant or fragments, as no functional limitation associated with the HGRA4sv variants or fragments in the claims. Therefore, it would require undue experimentation to practice this invention as claimed, because the skilled artisan would have no reasonable expectation of being able to use the HGRA4sv variants or fragments for any purpose stated in the specification. The specification provides neither clear direction or enough guidance, nor working example to teach how to use a commensurate number of the claimed species. As so, it is found that it would require undue experimentation to practice the invention in a manner commensurate in scope with the claim.

Claim 37 is further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is drawn to a polynucleotide having at least 97% sequence identity to SEQ ID NO:3 or the sequences encoding SEQ ID NO:4, or fragment thereof. The claim does not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making

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the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF’s were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated nucleic acid encoding the polypeptide comprising the amino acid sequence set forth in SEQ ID NO:4, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim 20 is further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the

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art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 20 states a deposit of a cDNA clone encoding said protein contained in ATCC Deposit No. PTA-2966. However, the specification fails to provide the deposit statement indicating the deposit material will be readily available to the public without restriction upon issuance of the patent. Such statement would satisfy the enablement requirement of 35 U.S.C. 112. For each deposit made pursuant to these regulations, the specification shall contain: (1) The accession number for the deposit; (2) The date of the deposit; (3) A description of the deposited biological material sufficient to specifically identify it and to permit examination; and (4) The name and address of the depository. (See MPEP 2404-2410.02)

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating

- (a) that the deposit has been made under the terms of the Budapest Treaty; **and**
 - (b) that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent,
- would satisfy the deposit requirements. See 37 C.F.R. 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then the requirements may be satisfied by an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or by a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and establishing that the following criteria have been met:

- (a) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;
- (b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;
- (c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

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(d) a viability statement in accordance with the provisions of 37 C.F.R. 1.807 is provided; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination, or loss of capability to function described in the manner in the specification.

In either case, the identifying information set forth in 37 C.F.R. 1.809(d) should be added to the specification if it is not already present. For deposits made with the ATCC, note that effective 23 March 1988 the depository's address is:

American Type Culture Collection
10801 University Boulevard
Manassas, VA 20110-2209

See 37 C.F.R. 1.803-1.809 for additional explanation of these requirements.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 is indefinite for the recitation of "the complimentary sequence (antisense)". It is unclear whether "antisense" in the parentheses is a part of the limitation of the claim, and if so, what limitation is imported by such. For example, does it eliminate other possible complimentary sequences such as complimentary DNA sequence (from the complimentary strand)? Therefore, the metes and bounds of the claim cannot be determined.

Claim 37 is indefinite for reciting a specific computer program "CLUSTALW global sequence alignment" as the claim does not specify the version number, and what parameters are to be used. Deletion of such a limitation is suggested as it adds no patentable weight to the claimed nucleic acid.

The remaining claims are rejected for depending from an indefinite claim.

Rejections Over Prior Art:

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20 and 30-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Grenningloh et al. (EMBO J. 1990 Mar; 9(3):771-6).

Grenningloh discloses a nucleic acid sequence (locus HSGLYRA1, Figure 1), which encodes a glycine receptor alpha subunit, and comprises nucleotide sequence encoding amino acid residues 247-302 of the instant SEQ ID NO:4 with 100% sequence identity (see the computer search result printout). Further, Grenningloh's nucleic acid is a cDNA clone (page 771, the right column), indicating the double strand of the molecule, and hence the complimentary sequence thereof. Although Grenningloh's nucleic acid sequence does not encode the entire sequence of the present SEQ ID NO:4, the nucleotide *fragment* encoding the cited amino acid fragment meets the limitation of "fragment thereof" in part (f) of claim 20, and claim 30, and is a "fragment thereof". As such, the reference anticipates claims 20 and 30. Additionally, the reference teaches an expression vector containing the nucleic acid, α 1-pCIS2 or pSPT19, and a host cell comprising the vector, HEK-293 (page 773). The reference, therefore, also anticipates claims 31 and 32.

Claims 20 and 30-32 are rejected under 35 U.S.C. 102(a) as being anticipated by Rappold-Hoerbrand, WO 00/58461 (provided by applicants).

Rappold-Hoerbrand discloses a nucleic acid sequence, SEQ ID NO:1, which encodes a human antaxia protein having SEQ ID NO:2, and comprises nucleotides 1-252 and 620-1321 of the instant SEQ ID NO:3 with 100% sequence identity (see the computer sequence search result printout). Further, the reference teaches that said nucleic acid sequence is a cDNA sequence indicating the double strand of the molecule, and hence the complimentary sequence thereof. Although Grenningloh's nucleic acid sequence does not encode the entire sequence of the present SEQ ID NO:4, the nucleotide *fragment* encoding the cited amino acid fragment meets the

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limitation of "fragment thereof" in part (f) of claim 20, and claim 30, and is a "fragment thereof". As such, the reference anticipates claims 20 and 30. Additionally, the reference teaches a recombinant vector and host cell containing the isolated nucleic acid (the paragraph bridging pages 9 and 10, and claims 7 and 8), and the reference, therefore, also anticipates claims 31 and 32.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 34-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grenningloh et al. (EMBO J. 1990 Mar; 9(3):771-6), or Rappold-Hoerbrand, WO 00/58461, as applied to claims 20 and 30-32 above, and further in view of Capon et al., US5,116,964.

The teachings of Grenningloh and Rappold-Hoerbrand are reviewed above. Neither reference teaches the nucleic acid further comprising a heterologous nucleotide sequence encoding the Fc domain of an immunoglobulin.

Capon discloses a novel polypeptide comprising an immunoglobulin Fc region, and a target protein sequence (column 5, lines 13-20). The cited reference indicates that fusion of a target protein to a stable plasma protein such as an immunoglobulin constant domain extends the

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in vivo plasma half-life, and facilitate purification of the protein (column 4, lines 38-43, and column 5, lines 13-20).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use the nucleic acid sequence of Grenningloh or Rappold-Hoerbrand to make a fusion polypeptide comprising said peptide and an Fc region as taught by Capon. One of ordinary skill in the art would have been motivated to make such a fusion polypeptide for the advantages taught by Capon, and reasonably would have expected success in view of Capon's disclosure, in which various genes had already been expressed successfully in their systems at the time the invention was made.

Conclusion:

No claim is allowed.

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Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

A handwritten signature in cursive script that reads "Lorraine Spector". The signature is written in black ink and is positioned above a rectangular stamp.

**LORRAINE SPECTOR
PRIMARY EXAMINER**

Dong Jiang, Ph.D.
Patent Examiner
AU1646
7/28/03